|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
NLM (National Library of Medicine ID: 101738825)
Index Copernicus Value 2019: 79.34
Volume 5, Issue 1; January: 2021; Page No. 60-62

Original Research Article

TO EXPLORE AND COMPARE BIOENHANCING ACTIVITY OF PIPERINE USING DIFFERENT ROUTES OF ADMINISTRATION (ORAL AND INTRAPERITONEAL)

Dr. Jitendra Gupta[1] & Dr. Apoorwa Gupta[2]

[1]Asst. Prof., Dept. of Pharmacology, Sri Aurobindo Institute of Medical Sciences & Research Centre, Indore, M.P.

[2]Consultant Microbiology, Apollo Hospital, Indore, M.P.

Article Info: Received 22 November 2020; Accepted 10 January 2021
DOI: https://doi.org/10.32553/ijmbs.v5i1.1620
Corresponding author: Dr. Apoorwa Gupta
Conflict of interest: No conflict of interest.

Abstract

Background & Method: The present study was conducted at Dept. of Pharmacology, Sri Aurobindo Institute of Medical Sciences & Research Centre, Indore. Piperine and was used to isolate the pure alkaloid, piperine, the extract was dissolved in 5 ml of ethyl alcohol. To this solution, 10 ml of 10% w/v of alcoholic potassium hydroxide was added with constant stirring. It was then filtered and allowed to stand overnight. The yellow needle shaped crystals of piperine were separated the next day.

Result: Pentazocine given in combination with piperine intraperitoneally showed significantly greater increase in reaction time as compared to pentazocine given in combination with piperine orally at 4 hr ($p < 0.05$). Sertraline given in combination with piperine intraperitoneally showed slightly greater increase in immobility period (58%) as compared to sertraline given in combination with piperine orally (51%), although not significant ($p > 0.05$). The oral combination of sertraline and piperine had significantly better activity than even the sertraline i.p. group ($p < 0.05$).

Conclusion: Studies are recommended on such combinations which may prove to be very good complimentary regimens for the treatment of many disorders. Pharmacokinetic studies are also required to further explore the bioenhancing property and characterise exact extent and mechanisms of such interactions.

Keywords: Piperine, Pentazocine, Sertraline & Albino Mice.
Study Designed: Observational Study.

Introduction

The black pepper (Piper nigrum Linn., 'Maricha' in Sanskrit) is one of the most renowned culinary spices. It is often called as the "King of Spices". It is native to the Malabar Coast of India and the island of Sri Lanka and has been known to Indian cooking since 2000 B.C. [1].

There are over 1,000 species of Piper plants, the nigrum being only one of them. Other species are Piper cubeba, used in medicine and to flavor cigarettes, Piper betel, whose leaves are chewed as a mild stimulant[2].

As already mentioned Black Pepper (Piper nigrum L.), a native South Indian spice belonging to the family Piperaceae, has been widely used in human diet for thousands of years. It is a flowering herb used mainly as a food adjunct, food preservative and insecticide. It is mainly valued for its characteristic sharp and stinging qualities making food palatable and giving it flavour, which are attributed to its chief alkaloid – PIPERINE[3].

In India the ground black pepper is commonly found on nearly every dinner table. Additionally it has also been a component of several preparations used in traditional medicine. The part of the plant mainly used for medicinal purposes, is the peppercorn or the fruit/berry[4]. Recent research has provided support for some of the traditional uses of pepper in medicine and has uncovered the probable mechanisms responsible for them.

Material & Method

The present study was conducted at Dept. of Pharmacology, Sri Aurobindo Institute of Medical Sciences & Research Centre, Indore from duration of Jan 2020 to Dec 2020.

Piperine and was used to isolate the pure alkaloid, piperine, the extract was dissolved in 5 ml of ethyl alcohol. To this solution, 10 ml of 10% w/v of alcoholic potassium hydroxide was added with constant stirring. It was then filtered and allowed to stand overnight. The yellow needle shaped crystals of piperine were separated the next day.

Swiss albino mice (20-30 g) of both sexes were procured from our central animal house. They were kept under standard environmental conditions of temperature, relative humidity and were fed with standardized diet and water ad libitum during an acclimatization period. The mice were fasted for 16 hours before experimentation but were allowed free access to water. Diabetes was induced by the injection of 150 mg/kg (i.p.) of alloxan monohydrate freshly dissolved in distilled water immediately before use.

Seventy-two hours later, the fasting blood glucose level in the mice was determined[5]. The blood glucose levels these animals were measured through tail clipping method using a one touch Glucometer device with strips. In this method the mouse was held in a mild restraining device and the distal 1 to 2 mm of the tail was clipped using a sterilized razor[6] and the droplet of blood collected directly on the glucometer strip. Only one droplet was sufficient for blood glucose determination on each occasion. Diabetes was further confirmed after 8 days and animals with fasting blood glucose of 6.0 mmol/L or more (100-300 mg/dl; moderately diabetic) were considered appropriate and employed in the study[7].

Results

Table 1: Effect of piperine on the analgesic activity of pentazocine given by different routes of administration, using the "Eddy's hot plate method"

Drug Treatment	Dose / Route	Reaction time in seconds				
		0 hr	0.5 hr	1 hr	2 hr	4 hr
Control 2 % Gum acacia	10 ml/kg, p.o.	3.00 ±0.27	2.80 ± 0.35	3.25 ± 0.38	2.87 ± 0.34	3.23 ± 0.30
Control 2 % Gum acacia	10 ml/kg, i.p.	3.13 ± 0.31	2.93 ± 0.24	3.19 ± 0.20	2.60 ± 0.33	3.48 ± 0.37
Pentazocine	5mg/kg, p.o.	2.95 ± 0.19	3.22 ± 0.17	4.93 ± 0.32	5.38 ± 0.53	3.98 ± 0.09
Pentazocine + Piperine	5 + 10 mg/kg, p.o.	2.58 ± 0.14	4.70* ± 0.33	6.52* ± 0.27	7.42* ± 0.28	5.43* ± 0.18
Pentazocine	5 mg/kg, i.p.	2.72 ± 0.20	3.43 ± 0.22	6.33* ± 0.28	6.57 ± 0.54	4.82 ± 0.26
Pentazocine + Piperine	5 + 10 mg/kg, i.p.	2.73 ± 0.20	3.90 ± 0.32	7.20* ± 0.45	8.33* # ± 0.54	6.60* # α ± 0.34
One way ANOVA	**F**	0.74	6.99	20.49	23.02	25.76
	P	> 0.05	<0.05	< 0.05	<0.05	< 0.05

Pentazocine given in combination with piperine orally showed significant increase in reaction time as compared to pentazocine alone (p.o.) group at 1,2 and 4 hrs ($p < 0.05$). Pentazocine in combination with piperine (p.o.) showed significant increase in reaction time at 0.5 hr as compared to control group ($p < 0.05$), whereas pentazocine alone (p.o.) did not ($p > 0.05$). Pentazocine given in combination with piperine intraperitoneally showed significantly greater increase in reaction time as compared to pentazocine alone (i.p.) group at 2 hr and 4 hr ($p < 0.05$). Pentazocine given in combination with piperine intraperitoneally showed significantly greater increase in reaction time as compared to pentazocine given in combination with piperine orally at 4 hr ($p < 0.05$).

Table 2: Effect of piperine on the antidepressant activity of sertraline given by different routes of administration, using the "tail suspension test" (TST)

Drug Treatment	Dose/Route	Period of immobility (in seconds) in 10 minutes
Control 2 % Gum acacia	10 ml/kg, p.o.	508.67 ± 19.83
Control 2 % Gum acacia	10 ml/kg, i.p.	494.50 ± 23.17
Sertraline	5mg/kg, p.o.	394.50 ± 17.29
Sertraline + Piperine	5 + 10 mg/kg, p.o.	244.67 ± 16.40* #
Sertraline	5 mg/kg, i.p.	315.00 ± 10.65*
Sertraline + Piperine	5 + 10 mg/kg, i.p.	204.83 ± 11.81* #
One way ANOVA	**F**	57.26
	P	< 0.05

Both the sertraline alone groups (oral and i.p.) showed significant increase in the immobility period as compared to the control groups; oral and i.p. respectively ($p < 0.05$). Both the sertraline and piperine combination groups (oral and i.p.) showed significant increase in the immobility period as compared to the sertraline oral and i.p alone groups respectively ($p < 0.05$). Sertraline given in combination with piperine intraperitoneally showed slightly greater increase in immobility period (58%) as compared to sertraline given in combination with piperine orally (51%), although not significant ($p > 0.05$). The oral combination of sertraline and piperine had significantly better activity than even the sertraline i.p. group ($p < 0.05$).

Discussion

The study on analgesic activity using the hot plate method shows that pentazocine given in combination with piperine, by both oral and intraperitoneal routes, gave significant better analgesic activity as compared to control and pentazocine given alone (oral and i.p. respectively), but at different time points described below. This was again a confirmation of the bioenhancing effects of piperine[8].

With the oral combination group, the improved analgesia, compared to the oral standard group, was evident as early as 1 hr, and remained for the entire duration of study i.e. 2, 4 hrs ($p < 0.05$). The oral combination also showed significant analgesia at 0.5 hr compared to control ($p < 0.05$), when the oral pentazocine alone group did not. This indicates that the oral combination group had a faster onset of action compared to the oral pentazocine group[9].

We conducted a similar study with the antidepressant drug sertraline which shows that both the oral and intraperitoneal combination groups of sertraline given with piperine showed better antidepressant activity than the control and respective standard groups (oral and i.p. respectively) ($p < 0.05$), thus confirming the bioenhancing effect of piperine with sertraline. Additionally, it was also seen that the effects of the oral combination were in fact better than sertraline given alone i.p. In other words the combination of piperine with sertraline by oral route makes it comparable to i.p. sertraline[10].

Conclusion

Studies are recommended on such combinations which may prove to be very good complimentary regimens for the treatment of many disorders. Pharmacokinetic studies are also required to further explore the bioenhancing property and characterise exact extent and mechanisms of such interactions.

References

1. Ramnaik Singh et al. Indian J Pharmacol. 2008 August; 40(4): 147–151.
2. http://en.wikipedia.org/wiki/Outline_of_The_History_of_the_Decline_and_Fall_of_The_Roman_Empire
3. Bharat B Aggarwal et al. Molecular targets and therapeutic uses of spices: Modern uses for ancient medicine.2009, World Scientific. P. 31-32.
4. Srinivasan K(2000).Spices: valued for more than taste and flavour of foods. In: Recent trends in spices and medicinal plants research (ed.) De AK. Associated Publishing Co., p 31-38.
5. Oladiende FO et al., Effect of Cnidoscolus aconite folius leaf extract on the blood glucose and insulin levels of inbred type 2 diabetic mice. Cell Mol Biol (Noisy-le-grand). 2007 May 15; 53(3):34.
6. Tuli JS, Smith JA, Morton DB. 1995. Corticosterone, adrenal and spleen weight in mice after tail bleeding, and its effect on nearby animals. Lab Anim 29:90–95.
7. Etuk, E.U., Animal models for studying diabetes mellitus. Agriculture And Biology Journal Of North America. ISSN Print: 2151-7517, ISSN Online: 2151-7525.
8. DeVane CL, Liston HL, Markowitz JS (2002). "Clinical pharmacokinetics of sertraline". Clinical Pharmacokinetics 41 (15): 1247–66.
9. Kobayashi K, Ishizuka T, Shimada N, Yoshimura Y, Kamijima K, Chiba K (1999). "Sertraline N-demethylation is catalyzed by multiple isoforms of human cytochrome P-450 in vitro". Drug Metab. Dispos. 27 (7): 763–6.
10. K.-W. Lee, H. Everts and A.C. Beynen. Essential oils in broiler nutrition. International Journal of Poultry 2004; 3 (12): 738-752.